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07/949,652	09/23/92	SIMONS	M-1647-6C-US

EXAMINER: M

TRAN, P

ART UNIT	PAPER NUMBER
1807	6

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18N1

DATE MAILED: 03/25/93

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☑ Responsive to communication filed on 9/23/92 and 1/19/93 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☑ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☑ Notice of Art Cited by Applicant, PTO-1449. (10 pages)
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☑ Claims 1-43 are pending in the application.
   Of the above, claims 28-34 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☑ Claims 21, 23-26 are allowed.
4. ☑ Claims 1-20, 22, 27, 35-43 are rejected.
5. ☐ Claims _____ are objected to.
6. ☑ Claims 1-43 are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev. 9-89)

07/AU 1807

15. Restriction to one of the following inventions is required under 35 U.S.C. § 121:

I. Claims 1-27 and 35-43, drawn to methods to detect DNA polymophism, classified in Class 435, subclass 6.

II. Claims 28-34, drawn to primers, amplified DNA, and kit comprising thereof, classified in Class 536, subclasses 23.1, 24.3 and 24.33.

The inventions are distinct, each from the other because of the following reasons:

Invention I and II are related as process of use and product. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case the product as claimed can be used in reverse transcription of a mRNA to which it is directed to, as a primer in a sequencing reaction of a cDNA or a genomic DNA encoding said mRNA, or as a probe to detect nucleic acids which hybridize thereto.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification as well as by their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

During a telephone conversation with Laura Terlizzi on March 5, 1993 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-27 and 35-43. Affirmation of this election must be made by applicant in responding to this Office action. Claims 28-34 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b), as being drawn to non-elected inventions.

16. The disclosure is objected to because of the following informalities:

(a) The journal references disclosed in Form 1449 are considered by the Examiner but would not be printed on a patent should one be issued from the instant application; the title of these references was not included in said form.

(b) The following claims are incorrect because they have a period following the denoted steps in the claims, e.g. claim 7. a.: Claims 7, 17, 20, 21, 22, 24, 26 and 27. Applicant is reminded that only a period following the claim number and an ending period are allowed in the claim. Amendment to the claims to recite the denoted step in parenthesis is suggested. Also, the steps in claims 22 and 24 should be denoted with letter numbers -i, ii, iii, etc.- instead of the alphabets because they have been used in the claims therefrom claims 22 and 24 depend.

(c) The numbers characterized the intervening sequences (IVS) should be amended to be cited in Roman numerals to be consistent with that recited in claims 21 and 26.

17. If applicant desires priority under 35 U.S.C. § 120 based upon a parent application, specific reference to the parent application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. Status of the parent application (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "Patent No." should follow the filing date of the parent application. If a parent application has become abandoned, the expression "abandoned" should follow the filing date of the parent application.

18. Claim 22 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 is vague and indefinite because it is not clear as to what the primers are. Although claim 21 (which claim 22 depends from) has already recited the primers being

specific to the IVS, claim 22 still recites "an HLA-locus specific primer". It is not clear whether applicant means a different pair of primer other than that recited in claim 21.

19. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph: it fails to teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure; the specification, as originally filed does not provide support for the invention as is now claimed.

20. Claim 27, step (b): applicant fails to recite combining amplified DNA sequence from said child's mother with endonuclease. Amendment to the claim to recite the deficiency; basis for such amendment should be pointed to in the specification.

Claim 27 is rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

21. Claims 1-6 are drawn to methods of detection yet fail to recite a detection step such as that recited in claim 7, step (b). The claimed invention is therefore not enabled as recited.

Claims 1-6 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

22. The new claims 35 and 36 recite a genetic locus having at least 4 (claim 35) or 8 alleles (claim36). The support for said matter as pointed out by applicant (page 15, lines 3-9 and lines 16-20) is not valid because the original specification discloses the 4 or 8 alleles for the HLA locus, not any locus; claim 1 (which claims 35 and 36 depend from) recites a general method, not method analyzing HLA.

Claims 35 and 36 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

23. The new claims 37-43 recite a method to analyze by identifying "sequence polymorphism" characteristic of the alleles. The support for said matter was not pointed out by applicant; the Examiner fails to locate such support in the specification. In light of Dr. Gresshoff's Declaration (paper dated 9/23/92), which discloses that he found site-specific polymorphisms on the sequence level, i.e. by sequencing the amplified sequence (page 3, second paragraph), the Examiner assumes that applicant's recitation of "sequence polymorphism" is that found and disclosed by Dr. Gresshoff in his Declaration. The Examiner fails to find any support for applicant's claiming "sequence polymorphism" in the original disclosure; therefore claims 37-43 are introducing new matter to the specification.

Claims 37-43 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

24. The new claim 38 recites "said non-coding region sequence is not more than about one kilobase in length". The support for said matter as pointed out by applicant (page 16, lines 16-26) is not valid because the pointed citation indicates that "the sequences are generally between about 1000 to about 2000 nt in length". Claim 38 is therefore introducing new matter to the specification.

Claim 38 is rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

25. The new claims 42 and 43 recite IVS 1, 2, 3 or 4 (for Class I) and IVS 1 or 2 (for Class II). The support for said matter as pointed out by applicant (page 43, lines 21-23) is not valid; the pointed citation discloses not the IVS but the variable exons: second and third exons for Class I; second exon for Class II. Claims 42 and 43 are therefore introducing new matter to the specification.

Claims 42 and 43 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

26. The allowed claims in the parent application (07/551239) were limited to HLA loci because the evidence or data presented therein was not sufficient to support broader claims, i.e. any other multi-allelic loci including the CF locus. Applicant intended to submit the declarations of experts stating that from the data provided by the inventor, the method was applicable to the CF gene, and therefore, was applicable generally (Paper dated 4/15/92, page 7, first full paragraph). Data applicable to the CF locus analysis have not yet been submitted by applicant; the only submission regarding the general application of the method is from Dr. Gresshoff ; the Declaration however is not applicable because it discloses that sequence polymorphism was found in the intergenic region, not in the intron or intron/exon regions as originally disclosed. In view of this, the Examiner is maitaining the original 112, 1st paragraph rejection made in the '239 application; a rejection on the newly introduced matter (the Declaration) is also being made.

Claims 1-16 and 37-41 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

27. Claims 17-20 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to the primer sites spanning a non-coding region sequence, and the primer pair defining a DNA sequence linked to the HLA locus. See M.P.E.P. §§ 706.03(n) and 706.03(z). The claims as recited are broad in scope (an allele of a HLA locus could be found in both the coding and non-coding region), which is not supported by the original disclosure: the polymorphism is found in the introns, not in any region of the HLA locus. Amendment to the claims to add limitation thereto as aforementioned is suggested.

28. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

29. Claims 17-20 are rejected under 35 U.S.C. § 103 as being unpatentable over Erlich (U.S. 4,582,788) in view of Saiki et al. (U.S. 4,683,194).

Claims 17-20 are drawn to methods to determine RFLP fragments of an HLA locus comprising an amplification and an endonuclease digestion step. Erlich discloses a RFLP HLA typing method (claim 1) and a nucleotide sequence of an HLA locus (clone 18C7 sequence in columns 9 and 10). Erlich fails to teach amplifying the locus instead of using whole genomic DNA for digestion. Saiki et al. disclose an amplification/RFLP method which comprises amplification of the target DNA and digestion thereof with restriction endonuclease (Summary of the Invention).

It would have been prima facie obvious to one of ordinary skill in the art to amplify a HLA locus before digestion for RFLP analysis because the HLA nucleotide sequence is known (Erlich) and PCR/RFLP method has been disclosed (Saiki et al.). An ordinary skill in the art would have known to make the invention because gene amplification by PCR for DNA analysis (RFLP for example) is much more sensitive and requires less starting amount of DNA than the conventional genomic digestion method.

30. No obvious double patenting rejection was made due to the terminal disclaimer filed by applicant (Paper dated 1/19/93).

31. Claims 1-16, 21-27 and 35-43 are allowable over the prior art of record. There is no prior art of record to teach or suggest the analysis of polymorphism using the information contained in the intron or non-coding region as disclosed in the instant application.

32. Any inquiry concerning this communication or those earlier from the examiner should be directed to Paul B. Tran, Ph.D. whose telephone number is (703) 308-2127.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose phone number is (703) 308-0196.

Paper related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). THe CM1 Fax Center number is (703) 305-3014.

Paul B. Tran, Ph.D.
3/16/93

AMELIA BURGESS YARBROUGH
PRIMARY EXAMINER
ART UNIT ~~187~~ 1807